

137. The isolated DNAs are excised, extracted or synthetic chemical compounds made by the hands of molecular biologist, not by nature. They are structurally distinct from any substance found in the human body—indeed, in all of nature.

138. Isolated DNA is different in kind, not merely different in degree of purity, from any composition found in nature. Isolated DNA acquires new properties not shared by its native counterpart. These new properties impart the isolated DNA molecules with new characteristics and new utilities. Unlike native DNA, the isolated form can be used as a probe, a diagnostic tool that a molecular biologist uses to target and bind to a particular portion of DNA, allowing it to be detectable using laboratory machinery. Native DNA cannot be used this way. Isolated DNA can also be used as another diagnostic tool, a “primer,” which is used in “sequencing” DNA, a method used by a molecular biologist to determine the primary structure of a DNA molecule. In sequencing, a primer binds to, or “hybridizes” with, a DNA target, such as a BRCA1/2 gene, DNA, or a synthetic DNA complementary to mRNA (“cDNA”) to form a hybridization product that acts as a substrate for the enzymes used in the sequencing reaction.

139. Native DNA does not have the chemical, structural, functional properties that make isolated DNA so useful to the molecular biologist. Native DNA cannot be used as molecular tools, such as probes and primers, and cannot be used to detect mutations. Nor can it be used in sequencing reactions to determine the structure of a DNA molecule. Excision, extraction, and purification from cellular components, or synthesizing DNA directly from its nucleotide components, is essential to be able to use the isolated DNA molecules as primers or probes. Thus, only isolated DNA molecules have the required chemical, structural and functional properties important for use as diagnostic tools and in the claimed diagnostic methods.

140. RNA cannot be used as a sequencing primer, because its chemistry is incompatible with performing as a sequencing primer.

141. Dr. Sulston's statement that “[t]he physical form in which [genetic sequences] occur is unimportant; what matters is the *informational content*” is thus inaccurate (see D. Sulston, ¶15). To the contrary, the physical form of a DNA molecule can significantly impact its function and the information it can yield.

**V. GENES ARE INEXTRICABLY LINKED TO OTHER COMPONENTS IN THE HUMAN BODY**

142. In the human body, genes are located on chromosomes. Historically, the term “gene” has been used to describe the unit that is responsible for the inheritance of a discrete trait, such as the color of peas in a peapod. In molecular terms, a gene is an aggregate of several segments of a chromosome. Some segments regulate the activity of the gene. From other segments, various types of RNA are produced. Types of RNA include tRNA, rRNA, and mRNA. From an mRNA template, protein is typically produced. In addition, the segments that make up one gene can be physically located adjacent to each other or apart on the chromosome.

143. The body does not have a mechanism “for isolating” genes, contrary what Dr. Jackson contends (see Jackson, ¶29). In the body, native DNA remains associated with chromosomes. Moreover, genes are also not like “mathematical algorithms” as Dr. Jackson proclaims (see D. Jackson, ¶47). This is because genes are *physical* entities, the functions of which are inextricably linked to their chemical composition and their interaction with other cellular components. Besides, the patents at issue in this case define an “isolated” nucleic acid as “substantially separated from other cellular components.” ‘473 Patent, col. 19:8-9.

144. In the human body, the 23 pairs of chromosomes are located in a cellular structure called the nucleus. Mitochondria, other cellular structures that convert food into energy, also contain a chromosome. A small fraction of human genes are carried by this mitochondrial chromosome. In humans, mitochondrial genes are maternally inherited because the mitochondria of an embryo are supplied by the egg but not by the sperm cell.

145. Cells divide throughout a person's life. The chromosomes, and with them genes and the DNA of which they are comprised, are also duplicated. The process of cell division takes place in the germline to generate egg and sperm cells. Cell division also takes place in the remaining, so-called somatic, cells of the body.

## **VI. RNA IS STRUCTURALLY AND FUNCTIONALLY DISTINCT FROM DNA**

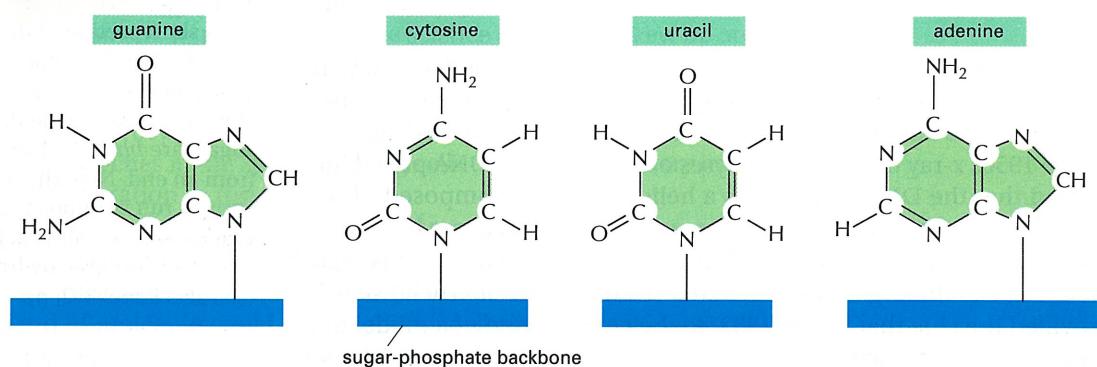
146. Like DNA, RNA – which stands for ribonucleic acid – is a chemical compound. Unlike DNA, however, the four bases that make up RNA are Guanine, Cytosine, Uracil, and Adenine. Thus, instead of the base Thymine, RNA contains Uracil. Common abbreviations of the bases of RNA are: “G” for guanine; “C” for Cytosine, “U” for Uracil, and “A” for Adenine. Each base together with one sugar and one phosphate molecule makes up one repeating unit known as a nucleotide of the RNA. Figure 6<sup>6</sup> below provides an illustration of the chemical structures of the four chemical bases of RNA.

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<sup>6</sup> Figure 6 is modified from a figure at page 100 of Alberts.

**Fig. 6**

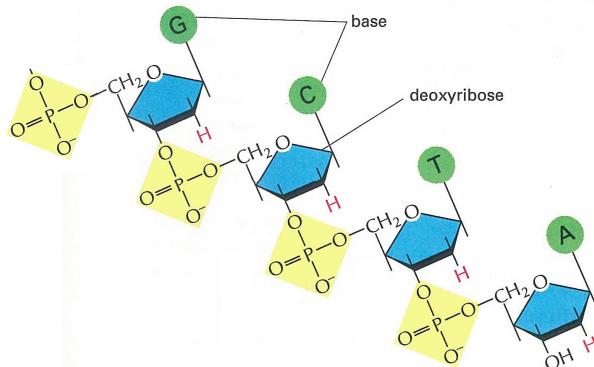
**FOUR BASES OF RNA**



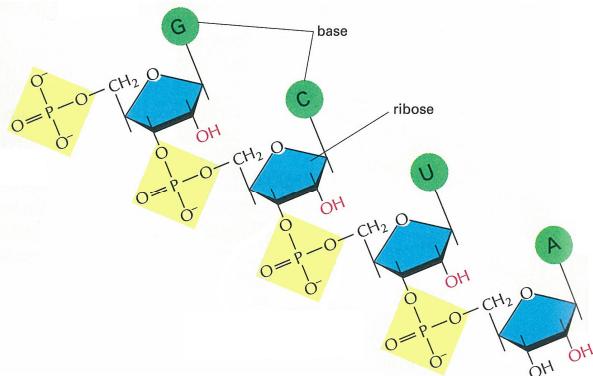
147. Also like DNA, RNA is formed by a strand of bases that are linked together via a sugar-phosphate backbone. The structures of the sugar-phosphate backbone of RNA and DNA, however, are different from each other—while RNA contains a ribose sugar, the sugar component of DNA is a deoxyribose. Figure 7<sup>7</sup> below is a depiction of the four bases of DNA and RNA, respectively, linked by a sugar-phosphate backbone.

**Fig. 7**

**SUGAR-PHOSPHATE BACKBONE OF DNA**



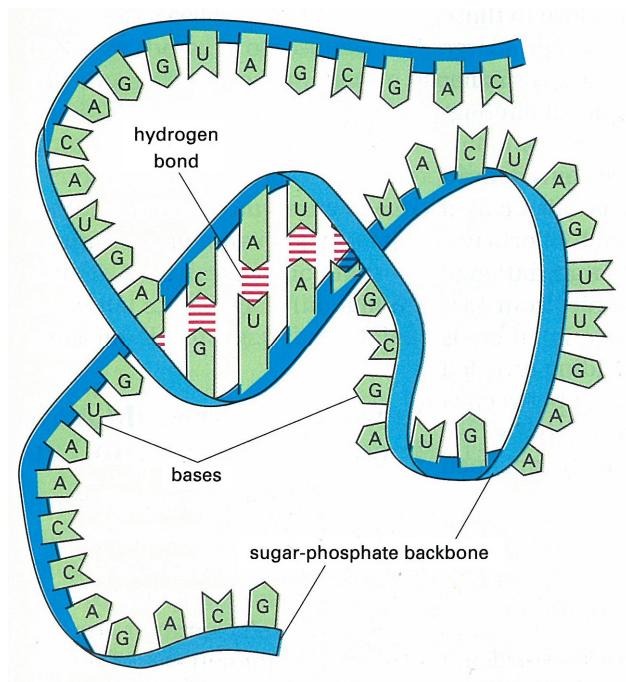
**SUGAR-PHOSPHATE BACKBONE OF RNA**



<sup>7</sup> Figure 7 is modified from a figure at pages 100 and 101 of Alberts.

148. The different structures of RNA and DNA affect their respective properties and functions. For example, unlike native DNA, which forms a double helix, RNA usually exists as a single strand. Like DNA in a cell, RNA is typically not found floating freely in solution. Cellular RNA is always bound to proteins. Further, DNA is a very stable molecule—DNA has been recovered from millennia-old fossils—whereas RNA, on the other hand, is much less stable. Even in the cell, RNA is sometimes degraded within hours of its generation. This difference in stability is one reason why isolated DNA molecules are more suitable for many biotechnology and diagnostic applications. Figure 8<sup>8</sup> below is an illustration of a single-stranded molecule of RNA.

**Fig. 8**



149. The process of RNA generation is called “transcription.” Many different RNA molecules are transcribed and processed from the native DNA of a chromosome. The

<sup>8</sup> Figure 8 is modified from a figure at page 100 of Alberts.

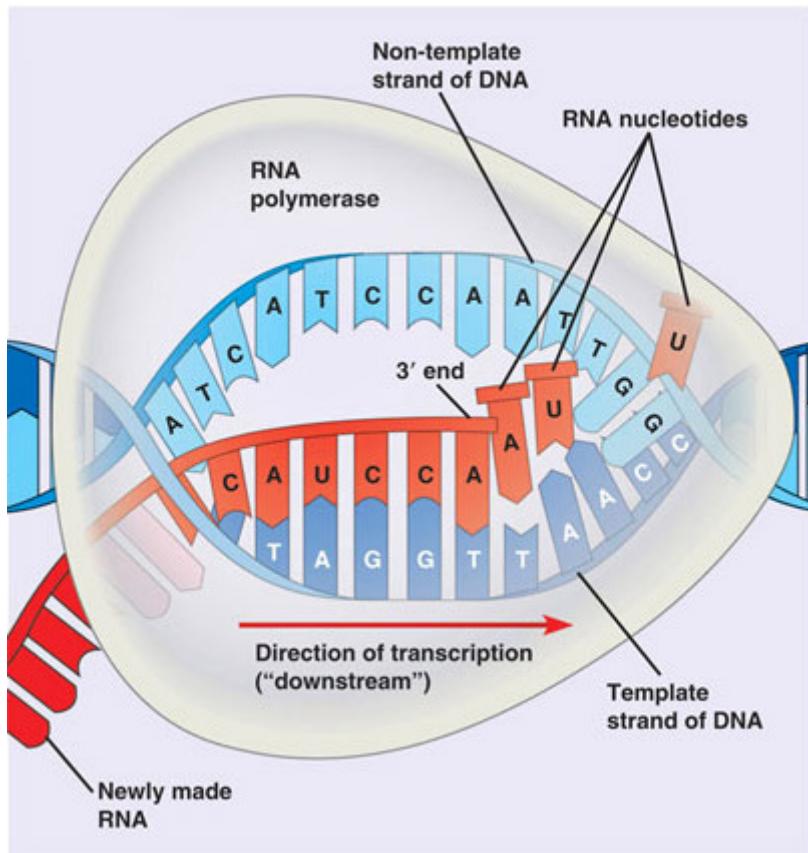
regulation of RNA transcription involves chromosomal segments that are usually not themselves transcribed into RNA. In fact, regulatory sequences can be at a very different location on the chromosome. These regulatory regions together with the region that is transcribed into RNA form a gene.

150. During transcription of RNA from DNA, a discrete segment of the DNA unwinds and the bases of the DNA molecule act as “clamps” that hold the bases of the newly forming RNA in place while the chemical bonds of the sugar-phosphate backbone are formed. This process is mediated by a structure in the cell known as the RNA polymerase. Adenine binds to Uracil, Thymine to Adenine, Guanine to Cytosine, and Cytosine to Guanine. Figure 9<sup>9</sup> below is an illustration of the process of RNA transcription from a DNA template strand.

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<sup>9</sup> Figure 9 is modified from a figure at the website of the Department of Biology of the University of Miami (<http://www.bio.miami.edu/~cmallery/150/gene/c7.17.7b.transcription.jpg>).

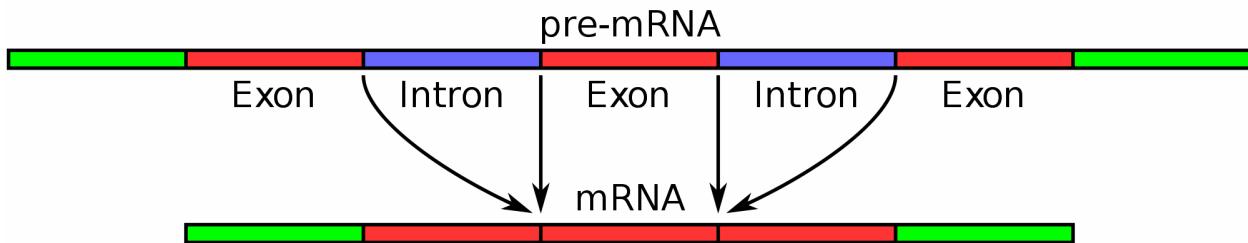
Fig. 9



151. A single gene may give rise to various different RNA molecules, which in turn may give rise to various different proteins. A newly transcribed RNA molecule (a “transcript”), or precursor messenger RNA (“pre-mRNA”), is processed to result in a mature messenger RNA (“mRNA”). Pre-mRNA contains nucleotides that are eliminated during a process called “splicing.” The segments of the pre-mRNA that spliced out are called introns (which can contain regulatory sequences), while the remaining segments, called exons, are ligated together. In addition, a chemical “cap” is added to one end of the RNA. A “tail” of nucleotides that contain the base adenine is added to the other end. The final mRNA molecule

contains only exons, a cap, and a poly-adenine tail. Figure 10<sup>10</sup> below is a simplified illustration of the process of pre-mRNA splicing to form mature mRNA.

**Fig. 10**



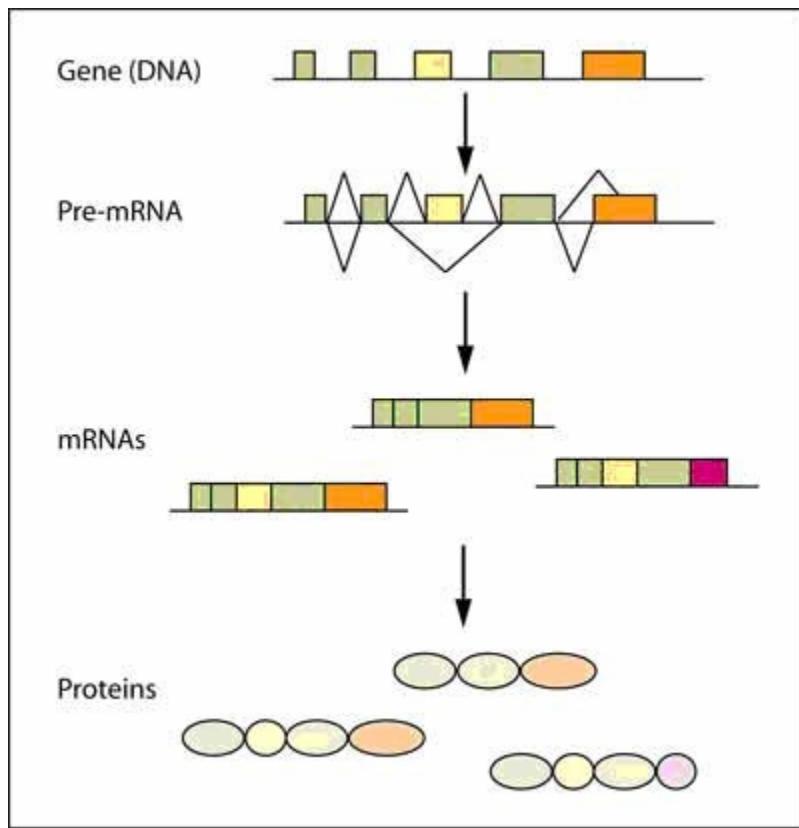
152. In addition, during a process called “alternative splicing,” different combinations of exons from the same pre-mRNA molecule can be spliced together yielding alternative mRNA products. Figure 11<sup>11</sup> is an schematic drawing of the process of alternative splicing.

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<sup>10</sup> Figure 10 is modified from the entry for “intron” at the online source Wikipedia.com.

<sup>11</sup> Figure 11 is modified from a figure at the website of the Scottish Crop Research Institute ([http://www.scri.ac.uk/scri/image/Research/genetics/genesanddevelopment/RNA\\_fig1.jpg](http://www.scri.ac.uk/scri/image/Research/genetics/genesanddevelopment/RNA_fig1.jpg)).

Fig. 11



153. Moreover, Dr. Grody's statement that "RNA will have the same (*i.e.*, complementary) nucleotide sequence as the DNA from which it is transcribed," is simply inaccurate because: (i) RNA is composed of different bases; (ii) the nucleotides in the RNA bind to the nucleotides in the DNA—they are not the same; and (iii) the RNA nucleotide sequence is modified by splicing, and adding of a cap and a tail of adenine. *See* D. Grody, ¶52.

154. Thus, contrary to Dr. Leonard's statement that "the coding effect of a cDNA is the same as that of the original DNA from which it was originally derived despite having a shorter sequence," alternative splicing can give rise to many different mRNAs from the same native DNA molecule (*see* Leonard, ¶75). cDNAs can be prepared from mRNAs as discussed

below. However, the cDNA captures that one mRNA from which it was synthesized and not all other splice variants that result from that one gene.

## **VII. PROTEINS ARE TRANSLATED FROM RNA**

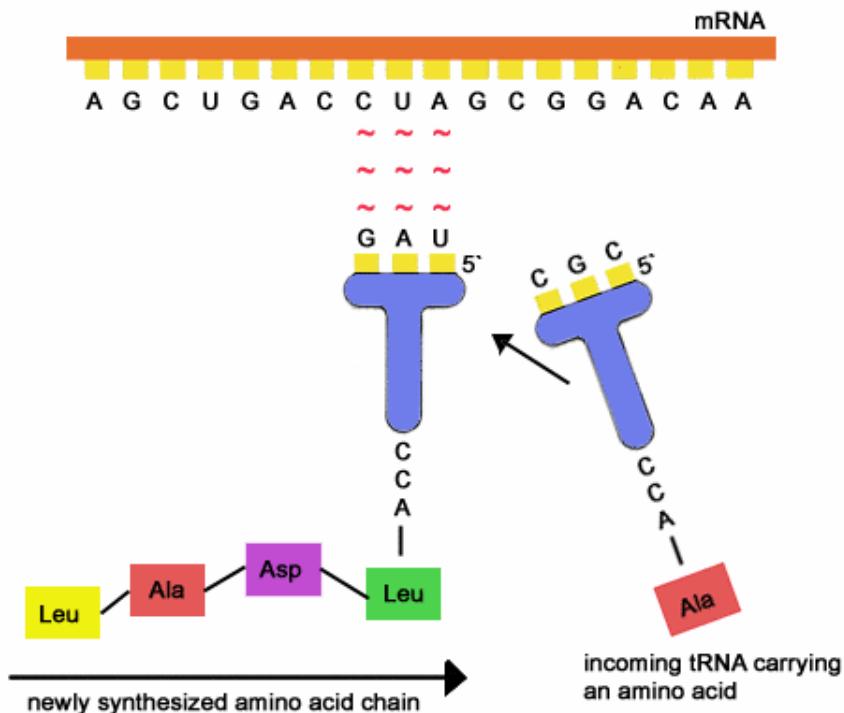
155. Proteins are generally large, complex molecules that play many critical roles in the body. They do most of the “work” in the body and are required for the structure, function, and regulation of the body’s tissues and organs.

156. Proteins are made up of hundreds or thousands of smaller units called amino acids, which are attached to one another in long chains. There are 20 different types of amino acids that can be combined to make a protein. The sequence of amino acids determines each protein’s unique 3-dimensional structure and its specific function.

157. Proteins are translated from mRNA through a process called “translation.” During translation, mRNA serves as a template to assemble a protein. Three consecutive bases in an mRNA molecule constitute a “codon,” which codes for one of the 20 amino acids. Pairing interactions take place between an mRNA molecule and another RNA molecule known as tRNA, which serves as an adaptor during protein translation. Specifically, sets of three nucleotides in the coding region of an mRNA, react with three nucleotides in a tRNA in such a way as to cause the amino acid linked to the tRNA molecule to be chemically transferred to the growing polypeptide chain destined to become a protein. The bases of the mRNA serve as “clamps” to hold the amino acids in place while the chemical bonds between the individual amino acids are formed. During translation, the mRNA template, the tRNA, the newly forming polypeptide chain, and the next amino acid reside in a multi-protein complex named ribosome. Once a protein is translated it typically undergoes post-translational modifications that are important for

the protein's function. Figure 12<sup>12</sup> below provides an illustration of the process of protein translation.

**Fig. 12**



158. The genetic code describes which codons code for which amino acids. For example, the codon Adenine-Thymine-Guanine encodes the amino acid Methionine. Thus, the chemical composition of an mRNA molecule determines the amino acid composition of a protein.

159. The genetic code is very much dependent on the cellular environment. For example, the three nucleotides Uracil-Guanine-Adenine do not encode an amino acid in the cytoplasm of a typical cell but it stops the process of translation so that the polypeptide is no

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<sup>12</sup> Figure 12 is modified from a figure at the website of the Genome Engineering Laboratory of the Institute for Bioinformatics at the National Yang Ming University, Taiwan (<http://gel.ym.edu.tw/~ycl6/sc2005/images/translation.gif>).

further extended. In mitochondria, however, the same codon encodes the amino acid Tryptophane.

160. I note that in his declaration, Dr. Sulston states that “it wasn’t until 1953—the year of the discovery of the structure of DNA—that we came to understand how DNA played its role.” D. Sulston, ¶13. I disagree. While the DNA double helix was originally suggested in 1953 by James D. Watson and Francis Crick, the genetic code was not elucidated until the early 1960’s. The physical structure of the DNA molecule by itself does not reveal how the DNA molecule functions. In fact, even knowing the nucleotide sequence by itself does not tell function.

### **VIII. cDNA, RNA, AND NATIVE DNA ARE STRUCTURALLY AND FUNCTIONALLY DIFFERENT FROM EACH OTHER**

161. Complementary DNA, or “cDNA,” is commonly synthesized from a mature mRNA in a reaction catalyzed by a protein known as reverse transcriptase. cDNA received its name because each base in the cDNA can bind to a base in the mRNA from which the cDNA is synthesized. In other words, it is “complementary” to the mRNA from which it is synthesized.

162. cDNA, as other isolated DNA molecules that are extracted, excised or synthesized, can be a useful tool for researchers as primers and probes in biotechnological and diagnostic applications. In the real world, virtually only synthetic DNA is used as primers and probes.

163. Moreover, when a scientist wants to express a specific protein in a cell that does not normally express that protein to learn more about the protein, the scientist can transfer the cDNA that codes for the protein to a recipient cell. If the cDNA is operatively linked to a

promoter that initiates transcription from the cDNA, the recipient cell will then express the protein of interest.

164. An isolated cDNA molecule is an artificial construct that does not exist in the body and hence is structurally and functionally different from both native DNA and RNA.

165. The method of cDNA construction helps to understand its multiple structural and functional differences from both native DNA and RNA. Several steps are required to construct a cDNA, involving many elegant molecular biology techniques. First, mature RNA is isolated from the tissues or cells of an organism. cDNA is then synthesized from the mature RNA using reverse transcriptase. In this process, the bases of the RNA serve as clamps while the chemical bonds between the nucleotides of the newly forming cDNA strand are formed. Uracil binds to and thereby acts as a clamp for Adenine, Thymine for Adenine, Guanine for Cytosine, and Cytosine for Guanine.

166. The synthesis of cDNA from very long mRNA molecules, such as *BRCA1* and *BRCA2*, often does not result in a cDNA strand that is as long as the mRNA chain. Instead, not unlike a puzzle, several cDNA fragments have to be pieced together to arrive at a composite full length cDNA. Initially, the cDNA is single stranded but the second strand can be synthesized to form a double stranded cDNA molecule.

167. Contrary to Dr. Mason's statement that "cDNA is simply a mirror of the RNA" and that "the functional sequence of the cDNA is identical to the functional sequence of the DNA," cDNA is both structurally and functionally different from RNA and from native DNA. cDNA is not mirror of mRNA nor is it identical to native DNA found in the body. *See* Mason, ¶29.

168. cDNA is *structurally* different from native DNA. First, cDNA made from an mRNA does not contain introns in contrast to native DNA, which contains many intronic sequences. Second, cDNA can contain sequences that correspond to the poly-adenine tail of mRNA, which does not exist in native DNA. Third, because it is not associated with proteins as with native DNA and because it lacks a 5' cap, no protein can be produced from an isolated cDNA molecule without introduction of regulatory sequences. Fourth, the sugar-phosphate backbone of native DNA is usually chemically modified, *e.g.*, by methylation. In contrast, the sugar-phosphate backbone of cDNA is not modified. Finally, as discussed above, isolated cDNA can serve as a probe, as a target for a probe, and as a template for a polymerase chain reaction (“PCR”), all of which native mRNA cannot do.

169. cDNA is also *functionally* different from native DNA. First, native DNA contains regulatory sequences. These regulatory sequences are not present in cDNA because they are not present in the mRNA from which the cDNA was synthesized. Second, because cDNA does not contain intronic sequences, mRNA can be transcribed from cDNA without the need for splicing. Third, introducing a cDNA alone into a cell does not give rise to protein production from that cDNA. Fourth, native DNA and chromosomal proteins form a functional unit; isolated or synthetic cDNA, however, is not associated with chromosomal protein and can thus be used as a molecular tool in various biotechnological applications.

170. As with native DNA, cDNA is *structurally* different from RNA, both pre-mRNA and mature mRNA. First, the set of bases in DNA is different from the set of bases in RNA. While the four bases in DNA are Adenine, Cytosine, Guanine, and Thymine, the four bases in RNA are Uracil, Adenine, Cytosine, and Guanine. Second, the sugar-phosphate

backbone in DNA is chemically different from the sugar-phosphate backbone of RNA. This difference in structure allows DNA to form the famous double helix.

171. cDNA is also *functionally* different from mRNA. First, cDNA is a much more stable molecule than mRNA. Second, protein can be translated directly from mRNA whereas protein cannot be directly translated from cDNA but requires the additional step of RNA transcription. Third, in the body, tens of thousands different mRNA molecules are present. Synthesized cDNA, on the other hand, is generated in the laboratory commonly as a homogenous population of molecules of the same kind to study the properties and functions of a specific gene of interest.

172. In addition to being structurally and functionally different from each other, native DNA and mRNA convey less information to researchers, as opposed to isolated DNA molecule such as cDNA. In its native state, the sequence of DNA or RNA molecule is almost like a mystery – they convey little or no information regarding their biological or clinical significance. Only upon isolation, synthesis, and complex analysis can this information become available to researchers and clinicians. Thus, isolated DNA is very much *informationally* different in kind.

**IX. ISOLATED BRCA1 AND BRACA2 cDNAS ARE SYNTHETIC, MAN-MADE COMPOSITIONS THAT ARE STRUCTURALLY AND FUNCTIONALLY DIFFERENT FROM NATIVE BRCA1 AND BRACA2 RNA AND DNA**

173. Isolated DNAs are structurally and functionally distinct from any DNA found in nature. The isolated *BRCA1* and *BRCA2* DNA molecules claimed in the *BRCA1* and *BRCA2* patents are likewise extracted, purified, or synthetic, and are structurally distinct from any substance found in the human body, or elsewhere in nature. For example, native DNAs are

physically connected to DNA regulatory sequences and proteins that determine which DNA sequences are expressed, how and where they expressed, and their level of expression. In contrast, the claimed isolated *BRCA1* and *BRCA2* DNAs are not associated with these regulators and do not contain this information.

174. As with isolated cDNA molecules described above, isolated *BRCA1* and *BRCA2* DNA molecules are typically man-made, synthetic molecules. They are structurally distinct from any substance found in the human body, or anywhere else in nature. Based on these structural differences, isolated *BRCA1* and *BRCA2* DNA molecules have very different functions and uses than native *BRCA1* and *BRCA2* RNA and DNA molecules. For example, isolated *BRCA1* and *BRCA2* DNA molecules can function as diagnostic probes and primers for detecting mutations, whereas native *BRCA1* and *BRCA2* RNA and DNA molecules cannot. Likewise, native *BRCA1* and *BRCA2* DNA molecules can pass genes from generation to generation, whereas isolated *BRCA1* and *BRCA2* DNA molecules cannot.

175. With regard to real world practical functions, isolated *BRCA1* and *BRCA2* DNA molecules can be used as primers for DNA sequencing to determine the chemical structure of a patient's *BRCA1* and *BRCA2* DNA sequence, respectively—native genes or DNA in a chromosome cannot be used for these functions.

176. Dr. Sulston states in his declaration that “[g]enetic sequencing is the process by which one ‘reads,’ or determines, the ordering of the 4 letters (A, T, C, and G) within a specified part of the genome.” D. Sulston, ¶ 20. However, sequencing is not simply “reading” a series of letters through a microscope. A DNA sequence cannot be determined by mere inspection. Instead, a series of extractions and chemical reactions must be performed.

177. In order to initiate a DNA sequencing reaction, at least part of the sequence of the target DNA molecule must be known. Plaintiffs fail to appreciate that sequencing of the *BRCA1* and *BRCA2* genes today is based on the breakthrough inventions that led to the patents at issue in this case, *i.e.*, the elucidation of the chemical structure of the genes and their association with an increased risk in breast and ovarian cancer.

178. To determine a DNA sequence of a patient for diagnostic purposes, a biological sample, such as a blood sample, from the patient must be processed. Native DNA or mRNA must be purified from the patient sample. The purification of native DNA of the entire genome, however, does not result in the purification of a single gene. Given that the DNA sequence of the human genome is over three billion nucleotides long, this initial purification step is still a long way from obtaining the sequence of a specific gene. To put things in perspective, the size of the *BRCA1* cDNA relates to the size of the entire genome approximately as a grain of sand to the height of the observation floor of the Empire State Building.<sup>13</sup>

179. Similarly, purification of mRNA from a patient sample yields a mixture of thousands or tens of thousands of different mRNA molecules. Even if cDNA is synthesized from this pool of mRNA molecules, the resulting cDNA molecules are similarly a mixture of thousands or tens of thousands of different cDNAs.

180. The standard method for sequencing DNA commonly used at the filing date of the patents was called the dideoxy sequencing method. Site-specific sequencing, as opposed to full length sequencing, is often used to identify an alteration at a specific nucleotide position.

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<sup>13</sup> For this analogy, I have used the following numbers: diameter of a grain of sand—0.6mm; height of the observation floor of the Empire State Building—320m; length of the cDNA of *BRCA1* in the ‘473 patent (SEQ ID NO:1)—5914 nucleotides; and size of the human genome—3,000,000,000 nucleotides.

181. To put things into perspective, one dideoxy sequencing reaction can provide the sequence of a DNA fragment that is about 300 nucleotides long. This is only 1/100,000 of one percent of the human genome! Thus, the sequencing reaction has to be initiated precisely at the target DNA sequence.

182. In his declaration, Dr. Jackson compares the process of extracting genes with the process of extracting paper pulp from wood. *See* Jackson, ¶19. *See also* Jackson ¶22. This analogy fails, however, because at least part of the sequence of the gene of interest must be known to allow the researcher or clinician to isolate and sequence the specific gene of interest.

183. To sequence a particular target, at least part of the target sequence must be known to design a suitable primer. The initial sequencing of a target sequence requires ingenuity far beyond the mere application of routine laboratory techniques and usually involves a significant amount of trial and error. A primer is used to initiate the sequencing reaction at the desired location of a target sequence. A primer is an artificial DNA fragment, usually between 15 and 30 nucleotides long, that binds specifically to the target nucleotide sequence. The nucleotide sequence of the primer is complementary to the target sequence such that the bases of the primer and the bases of the target sequence bind to each other. *See* Figure 5 above.

184. Target-sequence specific primers can also be used to initiate polymerase chain reaction (“PCR”), a technique that can be employed to isolate specific target DNA fragments for sequencing. For example, PCR can be used to synthesize a fragment of genomic DNA. The resulting fragment can then be sequenced. However, to do so, at least part of the sequence of the target DNA molecule must be known so that the target specific primer can be designed. Thus, the use of PCR requires knowledge of at least part of the target DNA sequence to design these

specific primers. In the case of *BRCA1* and *BRCA2*, for example, this knowledge has been provided by the inventors of the patents at issue in this case.

185. After diagnostic sequencing, the patient's sample, such as blood or tissue, is no longer blood or tissue but is has been processed to obtain DNA. The DNA has then been subjected to a sequencing reaction. At the end, instead of blood or tissue, the clinician has the chemical structure of a small portion of the patient's DNA.

186. The gene, mRNA and allele are in the body and must be obtained from a patient's tissue sample in order to be sequenced. The cells of the tissue sample must be broken open and a sample of DNA or RNA or allele extracted from the cells. cDNA can be synthesized using mRNA obtained from the patient sample. Various types of patient sample can be used, for example, a blood, tumor tissue, or non-tumor tissue. The DNA has to be isolated from these samples and put through sequencing reactions in order to obtain the sequence. This is transformative—the blood sample no longer resembles blood, and the patient's tissue no longer resembles the tissue.

187. The claimed diagnostic methods transform a deleterious gene buried among the over 25,000 other known genes in the human genome and make it detectable in the clinic. None of the method claims involve “looking” at genes. One cannot detect or determine a human subject's genes by mere inspection. Detection of a gene marker requires breaking open the cells of a tissue sample, and extracting and excising the native DNA. Using a set of molecular tools, such as a diagnostic probe or a primer that can specifically bind to a *BRCA1/2* DNA molecule in a tissue sample, the native DNA is analyzed to determine if the structural composition is the same or different from the normal native gene. These molecular diagnostic tools were designed

based on their ability to bind to and form a stable chemical structure with a target gene sequence. Thus, the claimed diagnostic methods are not mere abstract ideas, and cannot be performed by simply looking at a gene.

188. The nucleotide sequence of the human native DNA differs from person to person. Some alterations of the native DNA sequence have no known effects, while others may affect a particular trait, such as eye color. Other alterations may cause disease. Determining a DNA sequence and correlating it with pathological phenotypes can result in such life-saving diagnostics as Myriad's BRACAnalysis® test.

189. Alterations of genomic DNA sequences are inherited to the next generation if they occur in the germline. Alterations may also be caused by artificial environmental factors in somatic tissues. Such somatic alterations are normally not passed on to the next generation.

190. Without knowing the correlation between DNA sequence and a disease state, the nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Dr. Sulston himself has stated that: "The genome by itself does not provide answers to any of these questions." Sulston, 2002. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be painstakingly sequenced, analyzed, and correlated with the presence or absence of disease in the carrier of the sequence. This process can take many years.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: 12/21/09

A handwritten signature in black ink, appearing to read "Mark A. Kay".

Mark Allan Kay

## **LIST OF EXHIBITS**

1	<i>Curriculum vitae</i>
2	Dr. John E. Sulston, 2002, “Heritage of humanity,” <i>Le Monde diplomatique</i> , English Edition

**CERTIFICATE OF SERVICE**

This is to certify that on December 23, 2009, a true and correct copy of the foregoing document has been served on all counsel of record via the court's ECF system.

/s/ Brian M. Poissant  
\_\_\_\_\_  
Brian M. Poissant